

ABSENCE OF PLACENTAL GROWTH FACTOR AGGRAVATES DSS-INDUCED ACUTE COLONIC INJURY

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BACKGROUND: Angiogenesis has recently been described as a component in inflammatory bowel disease (IBD) pathogenesis. The vascular endothelial growth factor (VEGF) homologue placental growth factor (PlGF) establishes its angiogenic capacity during pathophysiological conditions. The role of PlGF in experimental colitis has never been investigated.

AIM: To investigate the role of PlGF in murine dextran sulphate sodium (DSS) colitis.

METHODS: Acute DSS colitis was induced in PlGF knock-out (-/-) and wild-type (WT) mice. Disease activity was calculated during the course of the experiment. Mice were sacrificed at several timepoints. Colonic injury was evaluated by colon length, intestinal epithelial apoptosis (TUNEL assay) and histological score. PlGF and VEGF were measured in distal colonic lysates by ELISA. Mucosal vascularization was quantified by computerized morphometric analysis of CD31 stained distal colonic sections. Intestinal hypoxia was visualized by pimonidazole staining and semi-quantitatively analysed by western blot for hypoxia inducible factor alpha (HIF-1 α).

RESULTS: During DSS colitis, PlGF-/- mice showed significantly increased disease activity ($P<0,001$), colonic shortening ($P=0,049$), colonic epithelial apoptosis ($P=0,025$) and histological damage score ($P=0,036$) compared to WT mice. DSS colitis was associated with a significant increase of PlGF (in WT mice) and VEGF (both in WT and PlGF-/- mice) in distal colonic tissue. Despite similar VEGF levels were reached in WT and PlGF -/- mice, the latter showed significantly less mucosal angiogenesis after DSS administration (mean vascular density: $P=0,046$, mean vessel diameter: $P=0,027$). This was associated with increased tissue pimonidazole uptake and accumulation of HIF-1 α .

CONCLUSION: Knock-out of placental growth factor strongly blocks angiogenesis during an acute mucosal injury associated with increased colonic hypoxia, and results in a worsening of the disease course.